15. The method of claim 1, wherein the target molecule is an MHC class I molecule, and the undesired immune reaction is tissue rejection during bone marrow transplantation.

16. The method of claim 13, wherein the cell is an antigen presenting cell.

17. The method of claim 13, wherein the cell is a B cell.

REMARKS

Attached hereto is an Appendix showing the changes made to the specification and claims 1 – 5 and 7, as amended.

Applicants have amended the Brief Description of the Drawings to reflect the numbering used in the Figures. These amendments do not introduce new matter and their entry is respectfully submitted.

Applicants have amended claims 1 and 5 to correct informalities objected to by the Examiner. These amendments are editorial in nature and do not introduce new matter; their entry is respectfully requested.

Applicants have amended claim 1 to more distinctly point out and claim the present invention. The amendment that indicates that the method is directed to a specific immune associate reaction. Support for this amendment is found throughout the specification, particularly at pages 1 – 3. Claim 1 has also been amended to indicate that the antibody binds to a target molecule. This amendment is supported throughout the specification, including for example at page 4, lines 4 – 20, and page 5, lines 24 – 29. As such, these amendments do not introduce new matter and their entry is respectfully requested.

Applicants have added new claims 13 – 17 to more particularly point out preferred embodiments of the invention. These claims are supported throughout the specification and examples. See particularly, page 7, lines 14 – 19, for claims 13 – 15 and page 13 for claims 16 - 17. Accordingly, these claims do not introduce new matter and their entry is respectfully requested.

The drawings were objected to as informal. Applicants are submitting herewith formal drawings, and have amended the Brief Description of the Drawings to reflect the

numbers used in the Figures. Accordingly, applicants respectfully submit that this objection has been obviated, and request its withdrawal.

The declaration was objected to as defective because there were non-initialed, non-dated alterations. Applicants are submitting herewith an amended, declaration (unexecuted copy attached). It is respectfully submitted that this objection should be withdrawn.

Claim 1 and Claim 5 were objected to because of certain informalities. Applicants respectfully submit that the amendments to these claims have obviated the objections, and their withdrawal is respectfully requested.

Claims 1 – 3 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the invention.

Applicants respectfully submit that the amendment to claim 1 has obviated the rejection, and its withdrawal is respectfully requested.

Accordingly, in view of the foregoing, applicant respectfully submits that all claims comply with 35 U.S.C. § 112, second paragraph.

Claims 1 – 5 and 7 were rejected under 35 U.S.C. § 102 (b) as being anticipated by Marasco et al., WO 94/02610.

Applicants respectfully submit that this rejection should be withdrawn for the following reasons.

Anticipation requires complete identity for every limitation. The present application explicitly teaches a method of inhibiting a specific undesired immune reaction by targeting molecules involved in that reaction. For example, an MHC class I molecule. But other target molecules are claimed. In this manner, one can eliminate the undesired immune reactions without preventing all immune reactions. This explicit method is the subject of the detailed description, the exemplification, and the claims of the present application. While WO 94/02610 teaches broad classes of all intracellular molecules as potential intrabody targets, one of which is the class of MHC molecules, WO 94/02610 does not specifically describe the exact specificity of immune response taught and claimed herein. Accordingly, the explicit embodiments of the present invention are in no way anticipated by the generic teaching of WO 94/02610. Accordingly, applicants respectfully submit that this rejection should be withdrawn.

Claims 1 – 5 and 7 were also rejected under 35 U.S.C. § 102 (e) as being anticipated by any one of three issued U.S. patents to Marasco: US 6,329,173 (the '173), U.S. 6,004,940 (the '940), and 5,965,371 (the '371).

The specifications of the '173 patent and the '371 patent are related applications and therefore are similar to each other as well as to the WO 94/02610. Accordingly, for the reasons above, the present application is not anticipated by the '173 or the '371 patent. The '940 patent, which is also generally directed to intrabodies, is specifically directed to vectors for binding transmembrane proteins, such as the IL-2 receptor. Applicants point out that the '940 is directed to **specific, preferred embodiments** which employ intrabody technology. The present application employs the intrabody technology and is able to provide specific immune regulation. This precise control of specific immune reactions, which permits one to maintain an immune system while not having the undesired immune reaction, is not explicitly taught by the prior art. Thus, there is no anticipation.

Accordingly, in view of the foregoing, applicants respectfully submit that claims 1 – 5 and 7 comply with 35 U.S.C. § 102.

Claims 1 and 7 were rejected under 35 U.S.C. § 103 (a) as being unpatentable over WO 94/02610 in view of Germain.

Applicants respectfully submit that this rejection should be withdrawn for the following reasons.

The combination of references does not suggest the precise control undesired immune reactions claimed. While WO 94/02610 is generic to the present invention, it does not teach the precise control of the present invention for MHC molecules, or for methods of inhibiting an undesired immune associated reaction. Germain merely provides a review of what was known at the time about the structure of MHC class I molecules, including the composition of two chains, a heavy chain and β2 microglobulin. The present invention is directed to the concept of regulating specific immune reaction by precisely targeting certain molecules but not others. Previous work established the general principles of intrabody technology, broadly describing how these novel antibodies are useful for targeting molecules expressed in different cellular compartments, including for example the nucleus, the ER, the cytoplasm, etc. The present invention uses intrabodies to much more precisely control native immunoregulation. One preferred embodiment provides inhibiting the transport of immunomodulatory molecules to the plasma membrane, thereby decreasing or

preventing a specific immune response. Another preferred embodiment uses intrabodies to target a processed certain peptides *before* they interacts with its receptor, thus blocking presentation of the peptide to the immune system altogether, and preventing the associated immune response. The present invention is explicitly directed to inhibiting such immune reactions by taking advantage of intrabody technology to target specific immunomodulators. Merely knowing the structure of MHC class I molecules, as provided by Germain, in no way renders this specific preferred embodiment obvious, because their structure does not provide the skilled artisan with the suggestion that intrabodies can be used to inhibit the immune system in this specific, directed manner. Thus, applicants respectfully submit that the present invention would not have been obvious to the skilled artisan. Accordingly, this rejection should be withdrawn.

Claims 1 and 7 were rejected under 35 U.S.C. § 103 (a) as being unpatentable over any one of the '173 patent, the '940 patent, or the '371 patent in view of Germain.

Applicants respectfully submit that this rejection should be withdrawn for all of the reasons presented above. As discussed, the combination of Marasco references teach a generic concept. Germain merely provides a review of the state of the art regarding the structure of MHC class I molecules. None of these references, alone or in combination, contemplates the explicit method of the present invention, namely inhibiting an undesired immune associated reaction by applying intrabody technology to specific components of the immune system, such as MHC class I molecules. Accordingly, this rejection should be withdrawn.

Accordingly, in view of the foregoing, applicants respectfully submit that claims 1 – 5 and 7 comply with 35 U.S.C. § 102.

In view of the foregoing, applicant respectfully submits that all claims are in condition for allowance. Early and favorable action is requested.

In the event that any additional fees are required, the PTO is authorized to charge our deposit account No. 50-0850.

Respectfully submitted,

Date: 1/27/03

Ronald I. Eisenstein
(Reg. No.: 30,628)
NIXON PEABODY LLP
101 Federal Street
Boston, MA 02110
(617) 345-6054

APPENDIX

The amendments to the claims are shown below, with insertions being underlined and deletions being bracketed.

IN THE SPECIFICATION:

Please substitute the following replacement paragraph for the paragraph on page 5, lines 8 – 11 of the above-identified application:

Figure 1 shows [Figures 1A and 1B show] a schematic illustration of MHC-1 surface expression, with the illustration on the left showing [Figure 1A shows] a normal pathway of MHC-1 cell surface expression, and the illustration on the right showing [Figure 1B shows] the cell surface expression in the presence of ER-expressed sFvhMHC-1.

Please substitute the following replacement paragraph for the paragraph on page 5, line 19 of the above-identified application:

Figures 5A and 5B show [Figure 5 shows] the FACS analysis of Jurkat stable subclones.

IN THE CLAIMS:

1. A method of inhibiting a specific undesired immune associated reaction comprising tranducing a cell that can be involved in the undesired immune associated reaction with a gene encoding an antibody, wherein said antibody when expressed will bind in the cell to a target molecule [molecules and/or ligand] involved in the undesired immune associated reaction, expressing the antibody and letting said antibody bind to said target molecule [receptor] and/or ligand].

2. The method of claim 1, wherein the target molecule [receptor] is selected from the group consisting of MHC class I molecules, MHC class II molecules, CD28 molecules, CD40 molecules, CD20 molecules and CD43 molecules.

3. The method of claim 1, wherein the target molecule [receptor] is selected from the group consisting of components in the pathways involving MHC class I molecules, MHC class II molecules, CD28 molecules, CD40 molecules, CD1 molecules, CD20 molecules, T cell receptors and CD43 molecules.

4. The method of claim 2 [1], wherein the antibody comprises a single chain antibody.

5. The method of claim 4, wherein the single chain antibody binds to an MHC I [MHC-1] molecule.